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Sex hormones modulate neurophysiological correlates of visual temporal attention

Cornelia Kranczioch[a,b,#], Anja Lindig[a,1], Markus Hausmann[c]

[a] School of Medicine and Health Sciences, Department of Psychology, Neuropsychology Lab, University of Oldenburg, 26111 Oldenburg, Germany

[b] Research Center Neurosensory Science, University of Oldenburg, 26111 Oldenburg, Germany

[c] Department of Psychology, Durham University, South Road, Durham DH1 3LE, United Kingdom

[#] Corresponding author

[1] Present address: Pius Hospital Oldenburg, Klinik für Hämatologie und Onkologie, Georgstraße 12, 26121 Oldenburg

Email addresses: cornelia.kranczioch@uni-oldenburg.de

anja.lindig@pius-hospital.de

markus.hausmann@durham.ac.uk

Abstract

The functional cerebral asymmetry (FCA) in processing targets within rapid serial visual presentation (RSVP) streams has been reported to fluctuate across the menstrual cycle, with identification of the second of two closely spaced targets being impaired when both targets occur in the left or the right hemifield stream during the luteal phase, while during the menstrual phase identification of the second target is only impaired for target pairs presented in the right hemifield stream. This fluctuation has been proposed to result from variations in estradiol levels. The current study used EEG to investigated whether the cycle-related fluctuation in RSVP target identification FCA relates to changes in early, stimulus-driven, bottom-up or in later, top down-driven aspects of FCA. While the former would be expected to become evident in the early visual evoked potentials (VEPs) P1 or N1, the latter would be evident in later event-related potentials (ERPs) such as N2pc or P3. Women performed a dual-stream RSVP task once during the menstrual phase and once during the follicular phase. Estradiol levels were determined from saliva samples. In contrast to previous findings, FCA in RSVP target identification was not affected by cycle phase. However, the impairment in second-target identification when targets where closely spaced was generally smaller during the menstrual phase than during the follicular phase. This effect was matched by shorter peak latencies of P1 VEPs for the menstrual phase, and by a reduction in the latency of the second-target P3 ERP for closely spaced relative to widely spaced target pairs, again for the menstrual phase. Results suggest that in a dual-stream RSVP setup, target identification, early stage stimulus processing, and target consolidation are affected by cycle phase, but that the asymmetry of these effects does not differ

between menstrual and follicular phase. The observed cycle-related modulations in neurophysiology and behavior could relate to the effects of estradiol on the locus ceruleus norepinephrine (LC-NE) system, which is known to play a major role in arousal, attention and stress response.

Keywords: RSVP, rapid serial visual presentation, attentional blink, AB, dual stream, VEP, ERP, functional cerebral asymmetry, estradiol, menstrual cycle

1. Introduction

Visual-temporal attention refers to the allocation of attention to target information presented in rapid succession with irrelevant information. In daily life such a situation can arise for instance when driving, playing computer games or watching TV. A widely used measure of visual-temporal attention performance is the Attentional Blink (AB). In the classic AB task, a series of stimuli is shown at fixation in rapid serial visual presentation (RSVP), which for this paradigm corresponds to a presentation rate of about 10 stimuli/second. The stream contains distracter stimuli and two pre-defined targets that need to be identified. A deficit in identifying the second target becomes apparent, if the two targets are closely spaced, that is, separated by about 200 to 400 ms or two to four temporal lags (Broadbent and Broadbent, 1987; Raymond et al., 1992; Weichselgartner and Sperling, 1987).

Over the past years, a large number of theories and models have evolved for explaining the AB (for reviews see Dux and Marois, 2009; Martens and Wyble, 2010). The neurocognitive models vary, with the AB for instance proposed to result from central capacity limitations for processing the targets (e.g., Chun and Potter, 1995; Isaak et al., 1999; Raffone et al., 2015; Vogel et al., 1998), from inhibition aimed at preventing in-depth processing of non-targets (Olivers and Meeter, 2008) or from overeager attentional control mechanisms that hamper the detection of a target as long as another target is being processed (Taatgen et al., 2009).

A number of studies have investigated the neurophysiological correlates of the AB. These studies revealed that early event-related potentials (ERPs), such as the P1 and the N1 components, which reflect perceptual processing in

stimulus specific areas of the visual cortex, are not reduced during the AB (Sergent et al., 2005; Vogel et al., 1998), suggesting that the AB is postperceptual in nature. Accordingly, the postperceptual ERP components N2pc and P3 clearly relate to the AB. The N2pc is a negative deflection above the visual cortex contra-lateral to the relevant stimulus. Its maximum is normally observed around 250 ms post stimulus. It is associated with attentional selection, and it specifically reflects selective processing of laterally presented stimuli (Eimer, 1996; Hickey et al., 2009). For the N2, the non-spatial equivalent of the N2pc, it has been shown that in the AB paradigm, it differentiates between seen and unseen second targets (Kranczioch et al., 2007; Sergent et al., 2005). The same holds true for the P3 (Kranczioch et al., 2003; Kranczioch et al., 2007; Rolke et al., 2001; Sergent et al., 2005), a positive deflection observed around 300 – 500 ms after target presentation. In the AB, the P3 not only reflects identification success (Verleger et al., 2011) and target consolidation (Sergent et al., 2005) but also resource sharing between the two targets. When the second target cannot be identified and an AB occurs, the P3 evoked by the first target tends to be larger as compared to when the second target is identified correctly (Kranczioch et al., 2007).

When two parallel RSVP streams are used, one in the left and one in the right visual field, instead of a single RSVP at fixation, a functional cerebral asymmetry (FCA) of visual temporal attention becomes evident. That is, the AB is reduced when the second target is presented in the left visual field stream (Holländer et al., 2005a; Shih, 2000), suggesting that the corresponding right cerebral hemisphere is less susceptible to AB.

However, there is compelling evidence that the degree of FCAs is sensitive to gonadal steroid hormones (i.e., estradiol and progesterone) and dynamically changes within relatively short time periods. For example, is has been shown that FCAs can fluctuate during the menstrual cycle in women (e.g., Hausmann, 2010; Hausmann and Bayer, 2010; Weis and Hausmann, 2010). Dynamic changes in the degree of FCAs have been shown for various lateralized cognitive domains, including language (Alexander et al., 2002; Cowell et al., 2011; Hampson, 1990a, b; Hausmann et al., 2002a; Hausmann and Güntürkün, 2000; Sanders and Wenmoth, 1998; Tillman, 2010; Wadnerkar et al., 2008; Weis et al., 2008), spatial cognition (e.g., Hausmann et al., 2002b; Hausmann and Güntürkün, 2000; Heister et al., 1989; Weis and Hausmann, 2010), and spatial attention (Hausmann, 2005; McCourt et al., 1997; Thimm et al., 2014). Given that visual-temporal attention, and the AB in particular, has also been found to be lateralized (Holländer et al., 2005a; Shih, 2000), it does not surprise that the FCA in the AB also fluctuates across the menstrual cycle (Holländer et al., 2005b).

Specifically, Holländer et al. (2005b) found that, during the midluteal phase, an AB occurred regardless of whether the two targets were presented in the left or right visual field stream. In contrast, during menses an AB occurred only when the two targets were presented in the right visual field stream. Additional regression analysis suggested that estradiol mediated this effect. The authors interpreted their results as being in line with the assumption of a hormone-related suppression of right-hemisphere functions during the luteal phase (Hampson, 1990a, b; Heister et al., 1989; Mead and Hampson, 1996; Sanders and Wenmoth, 1998). Although it is unclear which aspect or mechanism of right-hemisphere functioning is suppressed by estradiol, recent findings

suggest that estradiol reduces in particular the stimulus-driven bottom-up aspect of lateralization and inhibition (Hodgetts et al., 2015). Notably, this is in contrast to another finding of our group (Hjelmervik et al., 2012), suggesting that estradiol modulated especially top-down aspects of FCA.

The aspects of information processing contributing to the left visual field advantage in the AB task have been in the focus of several studies investigating its neurophysiological correlates. For N2pc evoked by the second target, it was found that the peak of this component occurred earlier when the second target was presented in the left visual stream (Verleger et al., 2011). Similarly, P3 amplitudes were larger in the left visual field condition. The same study also investigated visual evoked potentials (VEPs) evoked by the distracters presented at the beginning of each stream because this allowed to analyze the fundamental, stimulus-driven differences between RSVP processing in the left and the right hemisphere. The results revealed that earlier latencies for right hemisphere VEPs were evident. That is, FCAs were apparent in RSVP processing before target processing started. The results were interpreted as support for the idea that the right hemisphere has an advantage for structuring fast sequences, and that consequently participants are less susceptible to AB in the left visual field stream.

The aim of the present study was to investigate the neurophysiological correlates of the estradiol-related modulation of FCAs in visual-temporal attention. To this end, we tested normally cycling women in a dual stream AB task during the menstrual phase (low estradiol levels) and again during the follicular phase (high estradiol levels) and recorded the EEG. On the behavioral level, we expected a left visual field advantage for identifying the second target

(Holländer et al., 2005a; Shih, 2000; Smigasiewicz et al., 2010; Verleger et al., 2011; Verleger et al., 2009), in particular during the menstrual phase (Holländer et al., 2005b). When estradiol levels are high during the late follicular phase, we expected an increased AB in the left visual field, reflecting a more bilateral RSVP processing deficit (Holländer et al., 2005b). If found, this would support the idea that the right hemisphere advantage for RSVP processing is reduced when estradiol levels are high (Holländer et al., 2005b). For EEG data, and in line with previous reports, we hypothesized that the left visual field advantage is reflected in the distracter-evoked VEP and in the ERPs evoked by the second target (Verleger et al., 2011). If hemispheric differences were found to be reduced during the follicular phase for the distractor-evoked VEPs, this would indicate that estradiol affects the stimulus-specific aspects of AB lateralization (Hodgetts et al., 2015). If hemispheric differences were only affected for N2pc or P3, this would support the idea that estradiol primarily modulates the top-down aspects of AB lateralization (Hjelmervik et al., 2012).

2. Methods

2.1. Participants

Twenty-six women were recruited for the study. All women reported a regular menstrual cycle and did not currently, or in the previous 6 months, use hormonal contraceptives or other hormone regulating medications. They were free of current or past neurological or psychiatric illness. Participants had normal or corrected-to-normal vision. All participants gave informed consent

prior to the experimental sessions. Participants were paid a compensation of 8 Euro/hour. The local ethics committee approved the study.

Three women were excluded because they only participated in the first experimental session. Five participants were excluded based on atypical estradiol levels (see below, 2.2.2 Collecting saliva samples and hormone essays). In addition, five participants were excluded because their performance of correctly identified T1 was below 35.71% (20/56) of trials in any of the conditions. This threshold was derived based on a binomial test (Bortz et al., 2000) showing that for 56 trials, with respectively four response alternatives, 20 or more correct responses indicate significant above-chance performance.

Of the initial sample of 26 women, 13 women met all inclusion criteria. Mean age of the final sample was 28.3 years (SD=5.0). Mean cycle duration was 29 days (SD=2.1). All women were right-handed as determined by the Edinburgh Handedness Inventory (Oldfield, 1971).

2.2. Procedure

2.2.1. Planning of the experimental sessions

At least three consecutive cycles were monitored in order to plan the experimental sessions in accordance to individual cycle duration. Participants were then scheduled to participate in two experimental sessions. The testing order was randomized across participants. The first experimental session took place during the menstrual phase (cycle day 1-3, low levels of estradiol) or the follicular phase (cycle day 9-16, high levels of estradiol). For each participant, daytime of the two experimental sessions was kept constant to reduce potential

circadian influences. Of the final sample of 13 women, N=5 women were first tested in the menstrual phase and N=8 women were first tested in the follicular phase. Both subgroups did not differ with regard to age (menstrual-follicular M=28, SD= 4.1; follicular-menstrual M=28.5, SD=5.5; $t(11)=-0.18$, $p=0.43$), handedness (menstrual-follicular M=0.920, SD= 0.117; follicular-menstrual M=0.922, SD=0.112; $t(11)=0.034$, $p=0.49$) or daytime of testing (menstrual-follicular mean daytime of measurement first session 1:29 pm, mean daytime of measurement second session 1:37 pm; follicular-menstrual mean daytime of measurement first session 1:36 pm, mean daytime of measurement second session 1:22 pm).

2.2.2. Collecting saliva samples and hormone essays

Saliva estradiol was used as a previous study revealed estradiol levels to be significantly related to the lateralized AB. As mentioned above, five participants were excluded because of atypical estradiol levels. Of those, the estradiol level for one woman during the menstrual phase was below the limit of detection of 0.3 pg/mL of the hormone essay (Guidelines for Luminescence Immunoassay, IBL International, 2013). For two women estradiol levels during the menstrual phase were higher than during the follicular phase. For the remaining two women estradiol levels were only marginally higher (<50%) in the follicular than in the menstrual phase. Both women were first tested in the menstrual phase. Given that the late follicular phase is characterized by high estradiol levels, low estradiol levels indicate that cycle phase estimation based on day counts did not correspond with directly measured estradiol levels in

these women. This suggests either that the estimation of women's current cycle phase was inaccurate, or that these women experienced an anovulatory cycle. Atypical hormone levels might also suggest an endocrine disorder.

To facilitate collection of saliva samples, women were asked to avoid eating, drinking, smoking and brushing teeth for 30 min prior to the testing session. Two samples (2 × 1 ml) were collected directly before and after each test session. Women received small commercially available test tubes and were asked to fill them with saliva. The experimenter left the recording booth for the duration of saliva collection to ensure privacy. Saliva samples were stored at −20 °C until completion of the study. Saliva samples collected before and after each test session were blended before analysis in order to obtain an average estradiol concentration for each session. Samples were assayed by an independent professional hormone laboratory (IBL International GmbH, Hamburg, Germany) with commercially available 17β-estradiol luminescence immunoassays. The sensitivity of the assay was 0.3 pg/ml. The intra- and inter-assay coefficients were 13.3% and 14.8%, respectively.

2.2.3. Session layout

Both sessions started with participants filling in the State-Trait-Cheerfulness-Inventory (STCI-S <18>). The STCI-S assesses potential menstrual changes in mood state caused by gonadal hormones (Ruch et al., 1997), which has been shown to affect cognitive performance (Cockerill et al., 1994; Keenan et al., 1992; Reed et al., 2008; Schmitt et al., 2005). The STCI-S measures the concepts Cheerfulness, Seriousness and Bad Mood. However, no cycle-related

changes in mood were found in the present study: Cheerfulness: $t(12) = 0.45$, $p = .66$, Seriousness: $t(12) = 0.78$, $p = .45$, Bad mood: $t(12) = 1.04$, $p = .32$.

After STCI assessment, EEG measurement was prepared and participants were seated in a dimly lit, sound-attenuated booth. A 19-inch computer monitor (Belina BT10002) was mounted outside the booth at a viewing distance of about 190 cm. When comfortably seated, saliva samples were taken and participants received written task instructions.

2.3. Task and experimental setup

The experiment was run with Presentation software (Neurobehavioral Systems, 2010). A trial consisted of two streams of upper case letters presented in black that served as distracters. For each stream, letters were chosen from the alphabet without replacement and with the exception of the letters D, F, G, and K. Each trial contained two targets, in the following denoted as T1 and T2. The participant's task was to identify these targets. T1 was one of the letters D, F, G, K and was presented in white. T2 was one of the digits 2, 4, 7, 9 and was presented in black. All stimuli were presented in black on a grey background. The two target stimuli were either placed in the same stream (LL, RR) or they were placed in opposite streams (LR, RL). The opposite stream conditions were not of interest for the analysis of behavioral data or for ERP analysis but were included to ensure continued attendance of both streams. T1 was the sixth to tenth stimulus of one of the streams. T2 was either presented as the second (lag 2) of seventh (lag 7) stimulus following T1.

The two streams were presented synchronously and consisted of 22 stimuli each (cf. Figure 1). They were displayed left and right of a fixation cross that was presented at the center of the screen. The fixation cross was presented from 800 ms before onset of the streams and remained there for the duration of the streams. Participants were instructed to fixate the fixation cross at all times. The center-to-center distance between the two streams was 1.2 degrees of visual angle (Holländer et al., 2005b). Distracters and target stimuli were presented in Arial, font size 120 points. Presentation rate of the stimuli was 10 per second and stimulus duration was 50 ms.

Following the presentation of the two lateralized letter streams, a first response screen appeared prompting the participant to enter the identity of the letter (T1), this was followed by a second response screen prompting to enter the identity of the digit (T2). Responses were given via a custom keyboard. They were un-speeded and participants had to confirm their answers before the next trial would start. Participants were asked to guess, if they were not sure about the correct answer.

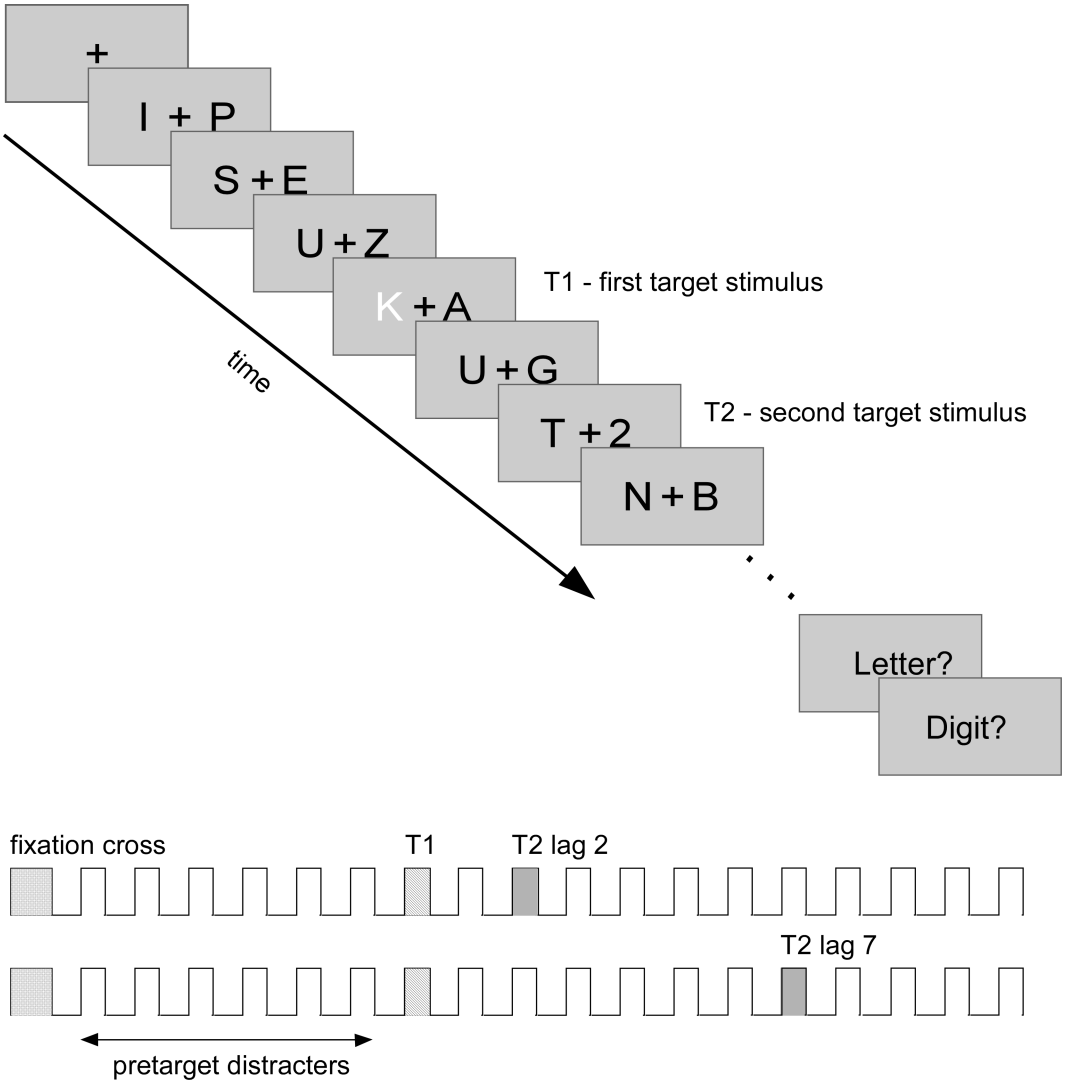

Figure 1. Schematic depiction of the trial layout.

In each experimental session, each hemifield condition (LL, RR, LR RL) was repeated 56 times, evenly split between lag 2 and lag 7 trials. Participants started each session with two short practice blocks. In the first practice block four trials were run at half speed. The second practice block consisted of 16 trials at normal speed. The main experiment consisted of seven blocks with 64 trials each. Each block contained eight trials per hemifield condition, respectively four

trials for lag 2 and four trials for lag 7. There was at least a 1 min break between blocks, after which participants initiated the next block.

2.4. EEG data collection and preprocessing

Electroencephalographic (EEG) signals were continuously recorded from 30 Ag/AgCl electrodes mounted on an elastic cap (EASYCAP GmbH, Herrsching, Germany) using a BrainAmp amplifier (BrainAmp, Brain Products GmbH, Gilching, Germany). Electrodes were positioned according to a customized equidistant layout (see Figure 2). A central, frontopolar channel served as ground. All channels were recorded against a nose-tip reference. Data were sampled at 500 Hz and recorded with a 0.016 Hz high-pass and a 250 Hz low-pass filter. Electrode impedances were kept below 20 kΩ.

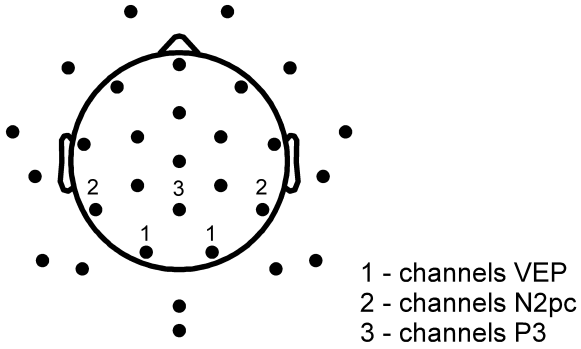

Figure 2. Electrode layout and channels for statistical analysis.

Data were analyzed offline using MATLAB (The Math-Works, Inc., Natick, Massachusetts, USA) and EEGLAB software (http://sccn.ucsd.edu/eeglab/, Delorme and Makeig, 2004). Independent component analysis (ICA) was used for

artifact correction (Jung et al., 2000). In a first step, original data were filtered using a 1 Hz high-pass filter and a 40 Hz low-pass filter. Data were segmented into 2-second epochs. Atypical and rare artifacts were automatically identified using routines from EEGLAB. The result was confirmed by visual inspection and contaminated epochs were rejected before running ICA. In a second step, ICA decomposition results were imported to the 0.1 to 20 Hz filtered data, and independent components (ICs) representing prototypical artifacts such as eye movements or ECG were identified and removed. For analysis of the visual evoked potentials (VEPs), cleaned data were segmented into 1500 ms epochs, covering a 100 ms baseline and the onset of the two streams. For analysis of T1 and T2 related ERPs, T1-locked epochs were created covering -100 to 1150 ms for T2 lag 2 trials and -100 to 1650 ms for T2 lag 7 trials. Epochs containing residual atypical and rare artifacts were again automatically identified using routines from EEGLAB and were rejected.

2.5. Data Analysis

VEPs were created by averaging all valid epochs irrespective of hemifield condition, T2 lag and T1 or T2 performance. Analysis focused on the VEPs evoked by pretarget distracters (cf. Figure 2) within the first 600 ms following the onset of the streams because the seventh stimulus could already be T1. Baseline was the 100 ms interval before the onset of the first distracter pair. Individual VEP amplitudes and latencies were measured automatically at a left and at a right occipital channel (see Figure 2). Epochs for extracting these measures were 75 ms long and were centered on the VEP peak latencies

identified in the grand mean averages. Grand mean average peak latencies were relative to the onset of each of the first six distracter pairs for P1 122 ms, 159 ms, 136 ms, 147 ms, 150 ms, and 157 ms and for N1 191 ms, 202 ms, 196 ms, 200 ms, 202 ms, and 205 ms. In contrast to latencies, amplitudes were not measured separately for P1 and N1 but jointly in a peak-to-peak measure. This was done to account for a slow drift evident in the data.

ERPs were created by separately averaging all valid epochs for the LL and RR conditions. Trials were only included in the averages, if both the T1 and the T2 responses were correct. Latencies and amplitudes of T1- and T2-related P3 were extracted from the averages of a cento-parietal channel. ERPs were baseline corrected with a 100 ms pre-target baseline. Peak amplitudes were semi-automatically measured at a centro-parietal channel (see Figure 2). In case no peak was identified by the algorithm peaks were identified manually. Search windows were based on visual inspection of the grand mean averages and were 200 to 500 ms post T1 for the T1-related P3, 450-750 ms post T2 for the P3 evoked by lag 2 T2 and 300 to 700 ms post T2 for the P3 evoked by lag 7 T2.

Latencies and amplitudes of T1-related N2pc were derived from difference waves for a left and a right parietal channel (see Figure 2). Differences were calculated within hemispheres but across hemifield conditions. That is, for condition LL, N2pc was calculated as [right channel LL – right channel RR] and for condition RR as [left channel RR – right channel LL]. To account for a different amount of shift in the different conditions, N2pc amplitudes were derived as peak-to-peak measures. The positive peak was measured in the 100-180 ms following T1. The negative peak was measured in the time range 170-

250 ms post T1. N2pc latency was measured in the negative peak. Peak measures were derived semi-automatically. In case the algorithm identified no peak, peaks were identified manually.

For T2 lag 2 trials, T2-related N2pc was derived following the approach used by Verleger et al. (2011). The first 700 ms of T2 lag 7 trials was subtracted from T2 lag 2 trials. For T2 lag 7 trials, this was not possible. Here, N2pc values were derived similar to the approach described for the T1-related N2pc. The resulting difference waves were baseline corrected with an interval covering the 200 ms before T2 presentation. This baseline was chosen to correct for random fluctuations that might occur in the pre-T2 time range. To improve signal-to-noise ratio in the T2-related N2pc measurements, amplitudes and latencies were measured in leave-one-out grand means, a method also known as the jackknife technique (Kiesel et al., 2008; Miller et al., 2009). Thirteen grand means were calculated, each based on 12 participants, so each grand mean leaving out one participant. Latencies were determined as the time point that divided the area-under-the–curve into equal halves, i.e. as the 50% area measure (Craston et al., 2009; Luck and Hillyard, 1990). The epochs for area-under-the-curve measurements were the 250-400 ms following T2 onset. In case the negative deflection did not span the entire epoch, any positive values were set to zero before calculating the area-under-the-curve values and determining the 50% area measure. Amplitudes were measured as mean amplitudes of the ±25 ms around the 50% area latency.

For statistical analysis, T2 identification performance was calculated based on all trials in which T1 had been correctly identified (T2|T1). T1

identification performance, T2|T1, N2pc and P3 latencies and amplitudes were analyzed with the same repeated measures ANOVA model that included the within-subject factors cycle phase (menstrual phase, follicular phase), hemifield condition (LL, RR), and T2 lag (lag 2, lag 7). For analysis of the T2-related N2pc, *F*-values were corrected for the diminished interindividual variance of the leave-one-out grand mean measurements. This was achieved by division of *F*-values by $(n-1)^2=144$ (Ulrich and Miller, 2001). VEP amplitudes and latencies were analyzed with a repeated measures ANOVA with the within-subject factors cycle phase (menstrual phase, follicular phase), distractor position (1, 2, 3, 4, 5, 6) and hemisphere (left, right). Significant interactions were followed up by additional ANOVAs or *t*-tests for dependent samples. *F*-values are reported with corrected degrees of freedom (Greenhouse-Geisser correction), if sphericity was violated (Mauchly's test).

To test whether any observed cycle-related behavioral or neurophysiological differences were correlated with estradiol levels, correlations were run with estradiol level as independent variable. Correlations were only run for the follicular phase because this cycle phase shows the largest variation in estradiol levels between participants. Estradiol levels during the menstrual phase are extremely low (i.e., close to the detection limit of the hormone assay) and show hardly any interindividual variability. For correlation analyses data were pooled across recording sessions. Prior to pooling, it was statistically confirmed that estradiol levels during the follicular phase did not differ between women tested in the first or second testing session, $t(11) = 0.65$, $p = .95$. Normality of the independent variable and of all dependent variables was tested prior to running correlations using Kolmogorov-Smirnov tests. Depending

on the results of normality testing Spearman or Pearson correlations were conducted.

3. Results

3.1. Salivary hormone concentrations

The mean saliva estradiol concentration (pg/mL) in the follicular phase (M = 3.95, SD = 1.67, range: 1.43 – 7.59) was significantly higher than those in the menstrual phase (M = 1.57, SD = 0.58, range: 0.75 – 2.36), $t(12) = 6.67$, $p < .0001$). The salivary hormone concentrations were comparable to previous reports using the same hormone assay as used in the present study (Hjelmervik et al., 2012).

3.2. Behavior

Statistical results are summarized in Table 1. No significant effects of the factors lag, hemifield, or cycle phase, or any significant interactions of these factors were observed for T1 identification. For T2|T1 significant main effects of lag, $F(1, 12) = 6.34$, $p < .05$, and hemifield condition, $F(1, 12) = 6.70$, $p < .05$, were observed, indicating that T2|T1 performance was generally better in hemifield condition LL and when T2 was presented at lag 7. These main effects were further specified by the significant lag × hemifield interaction, $F(1, 12) = 5.83$, $p < .05$. In spite of the overall better performance in hemifield condition LL, the difference between lag 2 and lag 7 was larger in hemifield condition LL, $t(12) = 2.94$, $p < .05$, than in RR, $t(12) = 1.17$, $p = 0.27$. Finally, the lag × cycle phase

interaction was significant, $F(1, 12) = 5.88$, $p < .05$[1]. Post-hoc *t*-tests indicated that the lag difference, that is, the AB, was only significant in the follicular phase, $t(12) = 3.25$, $p < .01$, not in the menstrual phase, $t(12) = 1.30$, $p = 0.21$. This is illustrated in Figure 3.

Table 1. Degrees of freedom, F-statistics, p-value, and effect size for each main effect and interaction for T1 and T2 identification rates. Means and SEMs are shown for each significant effect. P-values of significant effects are highlighted in bold.

Factors and interactions	df	*F*	*p*	ε^2	Mean (SEM) for significant effects
T1 identification					
lag	1,12	0.49	.50	.04	
cycle phase	1,12	0.40	.54	.03	
hemifield	1,12	0.24	.63	.02	
lag x cycle phase	1,12	<0.01	>.99	<.01	
lag x hemifield	1,12	0.10	.92	<.01	
cycle phase x hemifield	1,12	<0.01	.95	<.01	
lag x cycle phase x hemifield	1,12	0.27	.61	.02	
T2|T1 identification					
lag	1,12	6.36	**.03**	.35	lag 2 = 76.8 (3.8) %; lag 7 = 75.4 (3.3) %
cycle phase	1,12	<0.01	>.99	<.01	
hemifield	1,12	6.70	**.02**	.36	LL = 77.0 (3.6) %, RR = 66.2 (4.0) %
lag x cycle phase	1,12	5.90	**.03**	.33	men/lag 2 = 69.5 (4.7) %; men/lag 7 = 73.8 (4.0) % fol/lag 2 = 66.1 (4.2) %; fol/lag 7 = 77.1 (3.4) %
lag x hemifield	1,12	5.83	**.03**	.33	LL/lag 2 = 71.1 (5.0) %; LL/lag 7 = 83.0 (3.1) % RR/lag 2 = 64.5 (4.0) %; RR/lag 7 = 67.9 (4.7) %
cycle phase x hemifield	1,12	0.20	.67	.02	
lag x cycle phase x hemifield	1,12	0.34	.57	.03	

[1] This analysis was rerun including the two participants that did not fulfill the criterion that the estradiol level in the follicular phase should be at least 50% higher than in the menstrual phase. As might be expected, the interaction indicating an effect of cycle phase was slightly reduced with $F(1, 14) = 4.4$, $p = .054$, eta-squared = .24.

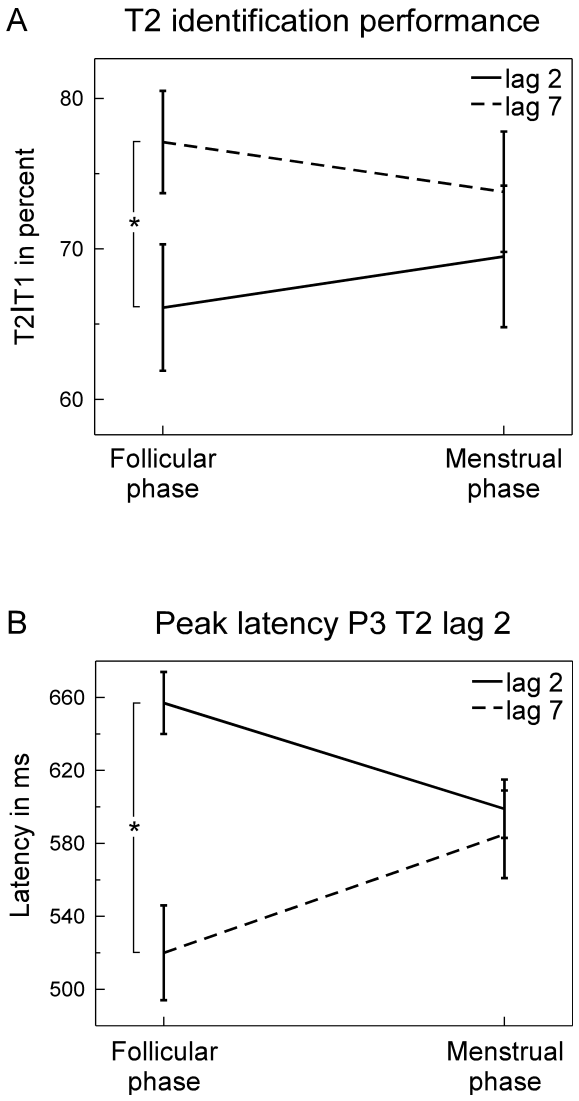

Figure 3. (A) Interaction of cycle phase and T2 lag for T2 identification performance. Error bars indicate SEM. The asterisk indicates a significant difference. (B) Interaction of cycle phase and T2 lag for T2 P3 peak latency. Error bars indicate SEM. The asterisk indicates a significant difference.

To explore whether the effect of cycle phase on the AB was modulated by test order (i.e., whether a given cycle phase fell into the first or the second experimental session), the ANOVA was re-run with test order (F1-M2, M1-F2) as additional between-subjects factor. A significant three-way interaction of lag, test order, and cycle phase ($F(1, 11)=7.8$, $p=.017$) was observed, which was followed up by a comparison of AB size between sessions 1 and 2 respectively for follicular phase (F1 and F2) and menstrual phase (M1 and M2) using

independent samples T-tests. AB size was calculated by subtracting T2 lag 2 performance values from T2 lag 7 performance values. During the follicular phase the AB was indeed larger for F1 than for F2 (F1: M = 16.3% vs. F2: M = 2.4%; $t(11) = 2.35$, $p = .04$). Crucially, the reverse was not the case for the menstrual phase. Here the AB was small and almost identical for first session and second session data (M1: M = 4.7% vs. M2: M = 3.5%), $t(11) = 0.17$, $p = .87$).

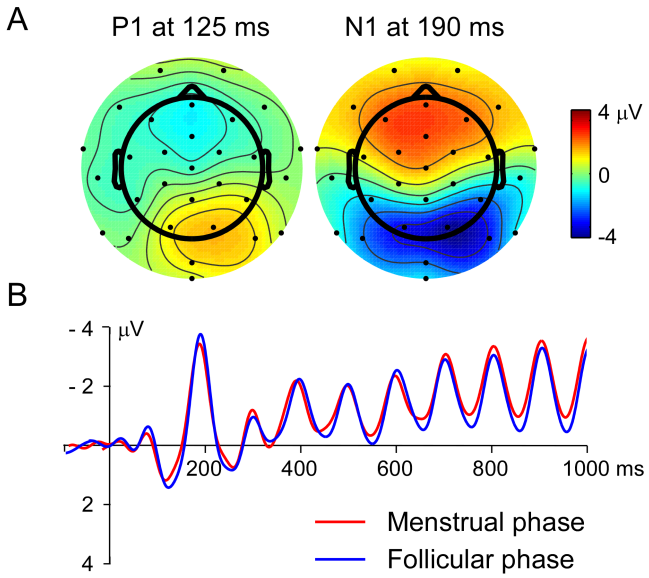

Figure 4. (A) Topographies of P1 and N1 for the first distracter in the RSVP stream. (B) VEPs evoked by the pretarget distracter stream averaged for the two occipital channels analyzed. Positivity is plotted down. P1 peaks earlier during the men- strual phase.

3.3. Visual evoked potentials to distracters

VEPs were evident in particular at occipital electrodes with an amplitude bias towards the right hemisphere (Figure 4A). The most prominent peak was the N1 in response to the first distracter pair (Figure 4B).

Table 2. Degrees of freedom, F-statistics, p-value, and effect size for each main effect and interaction for P1 latency, N1 latency, and P1-N1 amplitude. Means and SEMs are shown for each significant effect. P-values of significant effects are highlighted in bold.

Factors and interactions	df	*F*	*p*	ε^2	Mean (SEM) for significant effects
P1 latency					
distractor position	3.4,40.7	7.18	**<.001**	.37	positions 1 to 6: 130 (4) ms, 155 (5) ms, 140 (5) ms, 147 (5) ms, 150 (3) ms, 159 (3) ms
cycle phase	1,12	16.16	**.002**	.57	men = 144 (2) ms, fol = 149 (3) ms
hemisphere	1,12	0.47	.51	.04	
distractor position x cycle phase	2.3,27.2	0.74	.50	.06	
distractor position x hemisphere	3.0,36.0	1.70	.19	.12	
cycle phase x hemisphere	1,12	<0.01	.97	<.01	
distractor position x cycle phase x hemisphere	2.1,25.5	0.21	.83	.02	
N1 latency					
distractor position	2.6,31.1	3.18	**.04**	.21	positions 1 to 6: 194 (5) ms, 208 (4) ms, 200 (3) ms, 203 (4) ms, 208 (3) ms, 206 (2) ms
cycle phase	1,12	0.28	.61	.02	
hemisphere	1,12	2.80	.12	.19	
distractor position x cycle phase	2.5,30.2	0.88	.45	.07	
distractor position x hemisphere	4.0,47.7	1.37	.26	.10	
cycle phase x hemisphere	1,12	0.18	.68	.01	
distractor position x cycle phase x hemisphere	2.6,31.1	0.40	.73	.03	
P1-N1 amplitude					
distractor position	1.9,22.7	20.12	**<.001**	.63	positions 1 to 6: 7.4 (0.8) μV, 4.0 (0.5) μV, 4.2 (0.5) μV, 3.3 (0.4) μV, 3.5 (0.5) μV, 3.5 (0.4) μV
cycle phase	1,12	0.28	.60	.02	
hemisphere	1,12	4.10	.07	.26	
distractor position x cycle phase	2.4,28.6	1.40	.24	.10	
distractor position x hemisphere	2.2,26.9	0.51	.63	.40	
cycle phase x hemisphere	1,12	0.21	.65	.02	
distractor position x cycle phase x hemisphere	2.8,33.9	0.16	.91	.01	

Statistical results for VEP latencies and amplitudes are summarized in Table 2. On average, P1 latency was significantly shorter in the menstrual phase than in the follicular phase, $F(1, 12) = 16.16$, $p < .01$[2]. In addition, a main effect of distracter position was found, $F(3.39, 40.72) = 7.18$, $p < .001$. Latency increased linearly with distracter position with the marked exception of P1 for distracter position 2. Pairwise T-tests revealed that at this position latency was longer than

[2] The effect remained significant when the two participants that did not fulfill the criterion that the estradiol level in the follicular phase should be at least 50% higher than in the menstrual phase were included, F(1, 14) = 17.77, p =.001, eta-squared = .56.

at the preceding distracter position, $t(12) = 3.90$, $p < .01$, but also longer than at the following distracter position, $t(12) = 2.52$, $p < .05$. P1 latency was not significantly different between hemispheres, $F(1, 12) = 0.47$, $p = 0.51$. A subsequent exploratory ANOVA was run to test if the effect of cycle phase was modulated by the between-subjects factor test order (F1-M2, M2-F1). None of the interactions involving the factors cycle phase and test order were significant (all $F < 0.98$, all $p > .34$), indicating that this was not the case.

For N1 latency, the main effect of distracter position was significant, $F(2.59, 31.1) = 7.18$, $p < 0.05$, which is in line with the P1 latency. In contrast to P1 findings, however, pairwise *t*-tests between distracter positions 1-2 and 2-3 indicated that for N1 latencies distracter position 2 was not significantly different from distracter positions 1 [$t(12) = 2.16$, $p = .51$], and 3 [$t(12) = 1.96$, $p = .79$], respectively. Also, although N1 latency was numerically shorter over the right than left hemisphere electrode, this difference was not significant, $F(1, 12) = 2.80$, $p = .12$.

For P1-N1 amplitude, the mean effect of distractor position was significant, $F(1, 12) = 20.12$, $p < .0001$, indicating largest P1-N1 amplitudes for the first distracter pair, all $t(12) \geq 4.55$, $p \leq .001$. P1-N1 amplitudes further decreased with distracter position with a close-to-significant difference between positions 2 and 4 [$t(12) = 1.99$, $p = .07$], and significant differences between positions 2 and 6, 3 and 4, and 3 and 6, all $t(12) \geq 2.54$, $p < .05$. The main effect of factor hemisphere only approached significance, $F(1,12) = 4.10$, $p = .066$, indicating a trend towards larger amplitudes over the right than over the left hemisphere.

3.4. Event-related potentials

Irrespective of menstrual phase target processing was associated with a contralateral N2pc. In the contralateral-ipsilateral ERPs (cf. Figure 5), the N2pc showed well-defined peaks for T1 and for T2 when presented at lag 7. When T2 was presented at lag 2, the N2pc showed a less clear peak. The N2pc was most pronounced at left and right parieto-occipital electrode sites. N2pc was followed by a centro-parietal P3 (cf. Figure 6).

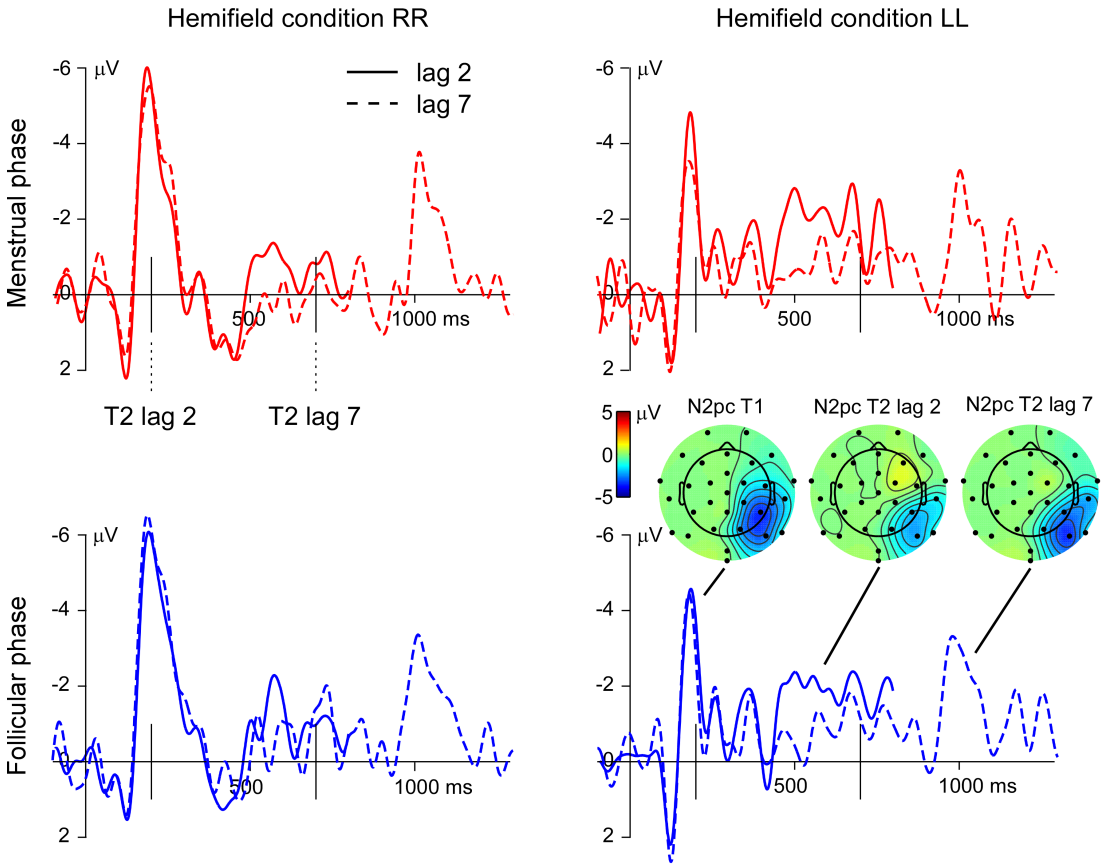

Figure 5. T1 and T2 related N2pc. Depicted is the contralateral-ipsilateral difference for the left parietal and the right parietal channels selected for statistical analysis (cf. Fig. 2) for hemifield condition LL and RR and menstrual and follicular phases. The bottom right plot (hemifield condition LL during the follicular phase) includes representative maps of N2pc topographies derived form the difference waves relative to target onset at 173–183 ms for T1, 310–320 ms for T2 lag 2, and 300–310 ms for T2 lag 7. Please note that the figure verifies the presence of N2pc for both targets and for both T2 lags during both cycle phases, it does not correspond to the ERPs used for statistical analysis.

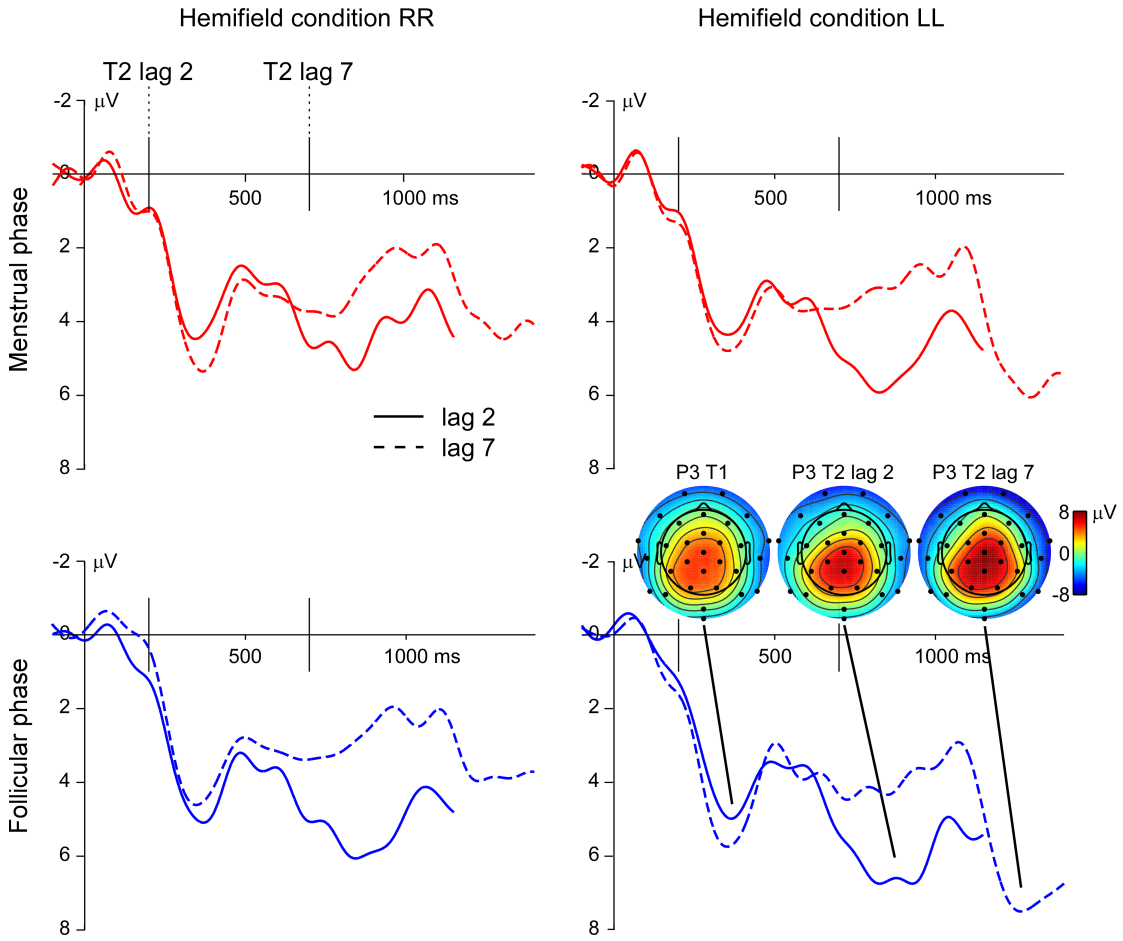

Figure 6. T1 and T2 related P3. ERPs are shown for the centro-parietal channel selected for statistical analysis (cf. Fig. 2) for hemifield conditions LL and RR and for menstrual and follicular phases. The bottom right plot (hemifield condition LL, follicular phase) includes representative maps of P3 topographies at 352–372 ms (T1), 631–651 ms (T2 lag 2), and 525–545 ms (T2 lag 7), respectively post target presentation.

3.4.1. T1-related N2pc and P3

Statistical results for T1-related N2pc and P3 latencies and amplitudes are summarized in Table 3. N2pc latency did not differ between T2 lags, cycle phases, or hemifield conditions, all $F < 3.36$, *ns*.

N2pc amplitude was larger in hemifield condition RR than in hemifield condition LL, $F(1, 12) = 5.64$, $p < .05$ (peak-to-peak amplitude 5.82 ± 0.86 mV vs. 4.68 ± 0.82 mV, respectively).

No other main effect or interaction was significant, all $F < 4.26$, *ns*. For P3 latency no significant main effects or interactions were observed for T2 lags, cycle phases, or hemifield conditions, $F < 4.29$, *ns*.

P3 amplitude did not differ between T2 lags, cycle phases, and hemifield conditions nor any interaction of the three factors, all $F < 3.66$, *ns*.

3.4.2. T2-related N2pc and P3

Statistical results for T2-related N2pc and P3 latencies and amplitudes are summarized in Table 3. N2pc latency was significantly shorter for hemifield condition LL than for hemifield condition RR as reflected in a main effect of hemifield condition, $F(1, 12) = 19.92$, $p < .001$. No other significant main effects or interactions were observed for factors T2 lag, cycle phase, or hemifield condition, all $F < 3.40$, *ns*, Table 4.

N2pc amplitude was more negative in hemifield condition LL than in hemifield condition RR, $F(1, 12) = 5.03$, $p < .05$. No other significant main effects or interactions were observed for factors T2 lag, cycle phase, or hemifield condition, all $F < 2.13$, *ns*.

Table 3. Degrees of freedom, F-statistics, p-value, and effect size for each main effect and interaction for T1 N2pc latency, T1 N2pc amplitude, T1 P3 latency, and T1 P3 amplitude. Means and SEMs are shown for each significant effect. P-values of significant effects are highlighted in bold.

Factors and interactions	df	*F*	*p*	ε^2	Mean (SEM) for significant effects
T1 N2pc latency					
lag	1,12	0.45	.52	.04	
cycle phase	1,12	0.39	.55	.03	
hemifield	1,12	0.06	.81	<.01	
lag x cycle phase	1,12	1.10	.32	.08	
lag x hemifield	1,12	3.36	.09	.22	
cycle phase x hemifield	1,12	0.02	.90	<.01	
lag x cycle phase x hemifield	1,12	0.14	.72	0.01	
T1 N2pc amplitude					
lag	1,12	1.28	.28	.10	
cycle phase	1,12	0.10	.76	<.01	
hemifield	1,12	5.64	**.04**	.32	LL = 4.7 (0.8) μV, RR = 5.8 (0.8) μV
lag x cycle phase	1,12	0.19	.67	.02	
lag x hemifield	1,12	0.33	.58	.03	
cycle phase x hemifield	1,12	1.03	.33	.08	
lag x cycle phase x hemifield	1,12	4.26	.06	.26	
T1 P3 latency					
lag	1,12	0.25	.63	.02	
cycle phase	1,12	0.82	.38	.06	
hemifield	1,12	0.73	.41	.06	
lag x cycle phase	1,12	4.29	.06	.26	
lag x hemifield	1,12	0.70	.42	.06	
cycle phase x hemifield	1,12	0.08	.78	<.01	
lag x cycle phase x hemifield	1,12	0.62	.45	.05	
T1 P3 amplitude					
lag	1,12	1.36	.27	.10	
cycle phase	1,12	1.03	.33	.08	
hemifield	1,12	0.71	.42	.06	
lag x cycle phase	1,12	0.65	.44	.05	
lag x hemifield	1,12	0.49	.50	.04	
cycle phase x hemifield	1,12	0.75	.41	.06	
lag x cycle phase x hemifield	1,12	3.67	.08	.23	

For P3 latency a main effect of lag was observed with latency for T2 lag 7 trials being significantly shorter than for T2 lag 2 trials, $F(1, 12) = 14.31$, $p < .01$. Moreover, and in line with the behavioral effect for T2|T1, a significant interaction between cycle phase and T2 lag was observed, $F(1, 12) = 9.05$, $p < .05$[3]: While T2-related P3 latencies did not differ between lags in the menstrual phase session, $t(12) = 0.72$, $p = 0.49$, T2 lag 2 P3 peaked significantly later than T2 lag 7 P3 during the follicular phase, $t(12) = 3.88$, $p < .01$. Finally, the hemifield

[3] The effect remained significant when the two participants that did not fulfill the criterion that the estradiol level in the follicular phase should be at least 50% higher than in the menstrual phase were included, $F(1, 14) = 6.79$, $p < .05$, eta-squared = .33.

× lag interaction was significant, $F(1, 12) = 6.62$, $p < .05$. The difference between P3 latencies evoked by lag 2 T2 and by lag 7 T2 was somewhat more pronounced in hemifield condition RR, $t(12)=4.0$, $p < .01$ than in hemifield condition LL, $t(12) = 2.11$, $p = .056$. A subsequent exploratory ANOVA was run to test if the interaction of lag and cycle phase was modulated by the between-subjects factor test order (F1-M2, M2-F1). The interactions involving lag, cycle phase, and test order did not reach significance (both $F < 2.97$, both $p > .11$), indicating that this was not the case.

For P3 amplitude, the main effect of hemifield was significant, $F(1, 12) = 8.62$, $p < .05$, with larger amplitudes for condition LL than RR. No other effect was significant, all $F < 4.51$, *ns*.

Table 4. Degrees of freedom, F-statistics, p-value, and effect size for each main effect and interaction for T2 N2pc latency, T2 N2pc amplitude, T2 P3 latency, and T2 P3 amplitude. Means and SEMs are shown for each significant effect. P-values of significant effects are highlighted in bold.

Factors and interactions	df	*F*	*p*	ε^2	Mean (SEM) for significant effects
T2 N2pc latency					
lag	1,12	0.09	ns		
cycle phase	1,12	2.72	ns		
hemifield	1,12	19.92	**<.01**		LL = 310 (0.3) ms, RR = 347 (0.6) ms
lag x cycle phase	1,12	0.27	ns		
lag x hemifield	1,12	0.51	ns		
cycle phase x hemifield	1,12	3.40	ns		
lag x cycle phase x hemifield	1,12	2.02	ns		
T2 N2pc amplitude					
lag	1,12	0.09	ns		
cycle phase	1,12	<.01	ns		
hemifield	1,12	5.13	**<.05**		LL = -1.8 (0.04) μV, RR = -0.7 (0.02) μV
lag x cycle phase	1,12	<.01	ns		
lag x hemifield	1,12	2.13	ns		
cycle phase x hemifield	1,12	<.01	ns		
lag x cycle phase x hemifield	1,12	<.01	ns		
T2 P3 latency					
lag	1,12	14.31	**.003**	.54	lag 2 = 627 (14) ms, lag 7 552 (17) ms
cycle phase	1,12	0.03	.87	<.01	
hemifield	1,12	0.72	.41	.06	
lag x cycle phase	1,12	9.05	**.01**	.43	
					men/lag 2 = 599 (16) ms; men/lag 7 = 585 (24) ms fol/lag 2 = 657 (17) ms; fol/lag 7 = 520 (26) ms
lag x hemifield	1,12	6.62	**.02**	.36	
					LL/lag 2 = 618 (21) ms; LL/lag 7 = 575 (20) ms RR/lag 2 = 638 (15) ms; RR/lag 7 = 529 (20) ms
cycle phase x hemifield	1,12	1.38	.26	.10	
lag x cycle phase x hemifield	1,12	0.05	.83	<.01	
T2 P3 amplitude					
lag	1,12	0.32	.58	.03	
cycle phase	1,12	3.95	.07	.25	
hemifield	1,12	8.62	**.01**	.42	LL = 7.4 (0.7) μV, RR = 5.7 (0.7) μV
lag x cycle phase	1,12	0.10	.75	<.01	
lag x hemifield	1,12	4.51	.06	.27	
					LL/lag 2 = 7.2 (0.7) μV; LL/lag 7 = 7.5 (0.9) μV RR/lag 2 = 6.2 (0.8) μV; RR/lag 7 = 5.3 (0.7) μV
cycle phase x hemifield	1,12	0.87	.37	.07	
lag x cycle phase x hemifield	1,12	3.64	.08	.23	

3.4.3. Correlation analyses

Correlation analyses were run with estradiol level as independent variable and the lag effect of T2 identification, P1 peak latency, and the lag effect of T2 P3 peak latency as dependent variables. Correlations were analyzed for the follicular phase only. The lag effects observed for T2 identification performance and for T2 P3 peak latency were quantified as the difference between individual lag 7 and lag 2 values. A Spearman correlation was run for estradiol level and the

lag effect of T2 P3 latency, for estradiol level and lag effect of T2 identification and for estradiol level and P1 peak latency Pearson correlations were conducted. No significant correlations were observed (all $r < |0.21|$, all $p > .5$).

4. Discussion

The present study aimed at investigating the effects of estradiol on task performance and the neurophysiological correlates of visual temporal attention as measured with the dual-stream AB task. Behavioral data confirmed the presence of FCA in this task, as identification performance for the second of two targets was generally better when targets appeared in the left visual field. The AB, that is, the difference in second target identification performance between short-lag and long-lag target pairs was, however, more pronounced for the left visual field. Results for distracter-evoked VEPs and T2-related ERPs were also in line with a LVF advantage for processing rapid stimulus sequences. Both behavioral and neurophysiological measures fluctuated across the menstrual cycle, though menstrual cycle did not affect the FCA in the AB task. Only for the follicular phase, a clear AB was observed. This effect was however not independent of order, that is, whether follicular phase data were collected in the first or second experimental session. In addition, a peak latency difference was present for the T2 P3 in the follicular phase, with longer latencies at lag 2 as compared to lag 7. P1 latency was longer during the follicular phase. In contrast to the effect observed for T2 performance both effects were not influenced by test order.

In line with previous research, the results of the present study confirmed the presence of an FCA in the dual-stream AB task (Holländer et al., 2005a; Holländer et al., 2005b; Verleger et al., 2011; Verleger et al., 2009). Results did not replicate the previously reported reduced AB when both targets are presented in the left visual field as compared to the right visual field (Holländer et al., 2005a; Holländer et al., 2005b). In the present study, a smaller AB would be reflected by a smaller difference between lag 2 T2 and lag 7 T2 identification for the left visual field. However, the opposite was observed. This may be explained by the fact that the AB reduction for left visual field targets is a less reliable finding than the overall left visual field advantage. For instance, Verleger and colleagues (2011; 2009) similarly observed a left visual field advantage with better T2 identification when T1 and T2 were presented in the left visual field as compared to the right visual field. This effect was however comparable for the short and the long target-to-target lags, that is, a lag-dependent effect indicative of a modulation of the AB for left visual field T2 was not observed.

The current study did not provide evidence for a fluctuation of FCAs in AB task performance across cycle phases. This is in contrast to Holländer et al. (2005b) who observed a reduced FCA in AB during the midluteal phase, which is defined by both high levels of estradiol and progesterone. Based on a regression analysis, Holländer et al. (2005b) concluded that the FCA in the AB was modulated by estradiol. The present study tested women during the menstrual and late follicular phases, the latter of which is defined by highest levels in estradiol and low progesterone levels. Therefore, the experimental setup of the current study allowed to test specifically whether high levels of estradiol alone are sufficient to modulate the FCA in the AB. The results of the present study

suggest that high estradiol levels alone are not sufficient to reduce FCA in the AB during the follicular phase. Although this finding is clearly in contrast to Holländer et al. (2005b) and our hypothesis, it should be noted that there is some evidence from the literature of estradiol alone (without progesterone) affecting both hemispheres similarly without altering FCAs (Dietrich et al., 2001; Hausmann et al., 2002a). For example, the fMRI study by Dietrich et al. revealed that high levels of estradiol in the follicular phase were related to an increase in the overall cortical activation of both hemispheres (see Hausmann and Bayer, 2010, for a review on this issue).

It is noteworthy that Holländer et al. (2005b) found a significant correlation between estradiol levels and the degree in AB FCA during the luteal phase. However, it cannot be fully ruled out that other hormones play a role too, such as progesterone and its metabolites, although progesterone levels were not directly correlated to FCA in Holländer et al.'s study. Other differences between studies that might have contributed to the divergent findings may be linked to differences in hormone essays. Holländer et al. (2005b) used blood samples, whereas the current study used saliva samples to determine estradiol levels which is assumed to better reflect the biological active, unbound concentrations of estradiol (Dabbs, 1990; Dabbs and Mohammed, 1992; Gavrilova and Lindau, 2009). Moreover, the inclusion criterion in Holländer et al. (2005b) was based on progesterone levels (midluteal at least 2 times higher than menstrual), whereas in our study it was based on estradiol levels. In other words, the current study should have been more sensitive to detect estradiol-related effects.

In the present study the AB was small during the menstrual phase, irrespective of whether the menstrual phase fell into the first or the second experimental session and irrespective of whether targets were presented in the left or the right visual field. This was different for the follicular phase where a considerable AB occurred during the follicular phase when it fell into the first experimental session, but nearly no AB was evident when the follicular phase fell into the second experimental session.

It could be argued that the observed pattern of results indicates that cycle phase was confounded with test order, that is, that of the final sample more women were first tested in the follicular phase first than were tested first in the menstrual phase, and that therefore the menstrual phase data set simply contains more second session data. However, that the AB was *not* generally larger for the first experimental session argues against the possibility that only test order, and therefore task practice, could be responsible for the observed effect of cycle phase on the AB. In line with this conclusion, for a moderate number of sessions a reduction of the AB is generally not reported (Choi et al., 2012; Kranczioch and Thorne, 2013; but see Taatgen et al., 2009 for some evidence of a potential reduction of the AB at the beginning of an experimental session), though it has been shown that after an average of 15 sessions of the AB task a significant reduction of the AB can be found (Maki and Padmanabhan, 1994). In contrast, a rather consistent finding is an improvement of T2 performance that is however importantly not specific to the AB lag(s)(Kranczioch and Thorne, 2013; Nakatani et al., 2012; Seiffert and DiLollo, 1997). A second argument against the confounder of cycle phase with test order is that including two women in the sample that did not fulfill our strict inclusion

criteria but that were both first tested in the menstrual phase did, as one would expect, reduce but not fundamentally change the observed effect of cycle phase on the AB. In sum, we believe that a confounder of cycle phase with test order is rather unlikely.

Nevertheless, the effect of test order on the interaction of lag and cycle phase requires some explanation. One could argue that the group that started testing during the menstrual phase coincidently consisted mainly nonblinkers, that is, people that do show no or only a very small AB in their first AB experiment and when repeatedly tested (Martens et al., 2006). In an experimental design as the present one these true nonblinkers would be expected to stay nonblinkers in the second experimental session. Yet even though we cannot completely rule out the possibility that by chance only nonblinkers remained in the group that started testing during the menstrual phase, this is very unlikely. One reason for this conclusion is the low probability of recruiting a nonblinker - not even 8% of participants can be expected to be nonblinkers (Martens et al., 2006). A second reason is that nonblinkers show neurophysiological differences from blinkers, most evidently a shorter P3 peak latency (Martens et al., 2006). Such difference was, however, not evident in the present study. The results rather indicate a carryover effect, that is, a cycle-related reduction in the AB when women were tested first in the menstrual phase. Processing rapidly incoming information was particularly good during the menstrual phase, irrespective of test order. This is supported by the overall shorter peak latencies of the P1 and of the lag 2 T2 P3 during the menstrual phase than during the follicular phase. In contrast, when participants were first tested in the follicular phase (high levels of estradiol), performance was

particularly low. However, if the follicular test session followed the menstrual test session the good performance from the menstrual test session apparently carried over to the follicular test session and women would be likely to continue to perform well in spite of the unfavorable effect of estradiol. This interpretation is well in line with the finding that, if the AB is experimentally eliminated by making T2 color-salient for a limited period of time, the AB will not reoccur when the color-saliency is removed (Choi et al., 2012). The mechanisms underlying the continued good performance for the follicular phase appear however to be different from those reflected in P1 and lag 2 T2 P3 peak latencies, because both measures were longer during the follicular phase than during the menstrual phase irrespective of test order (interactions including cycle phase and test order all $F < 0.98$, all $p > .34$). Carry-over effects in menstrual-cycle studies have been reported before. For example, it has been shown that cognitive performance can increase when participants are initially tested in an estradiol-related conducive state, compared to those who began testing in a less favorable hormonal state for a particular task (Hampson, 1990b; Mead and Hampson, 1996).

Assuming that the observed cycle-related differences in AB task performance are indeed related to the menstrual cycle, they might result from the influence of estradiol on the activity of the locus coeruleus (LC). The LC-norepinephrine (LC-NE) system is known to play a major role in arousal, attention and stress response (Benarroch, 2009). One hypothesis of the AB suggests that the AB is mediated by the activity of the LC-NE system. According to this idea, T2 tends to be missed at intermediate lags because its presentation coincides with the refractory period in LC activity that follows the LC phasic

response elicited by T1 (Nieuwenhuis et al., 2005). Though an empirical test of this idea did not provide supporting evidence (Nieuwenhuis et al., 2007), an indirect link between LC activity and the AB might still exist, and this link might be mediated by estradiol. From animal studies it is known that estradiol affects LC activity (Centeno et al., 2006; Östlund et al., 2003; Szawka et al., 2009), and one might assume that the behavioral pattern observed here is, at least in part, a result of the effect of high estradiol levels on the LC-NE system. Reports are inconsistent though with regard to the direction of the effect of estradiol. While Szawka et al. (2009) suggested that estradiol inhibited the activity of the LC-NE system, others reported that estradiol can increase LC activity and NE release (Centeno et al., 2006; Östlund et al., 2003). Irrespective of the direction of the effect, our data suggest that, if the effect of estradiol on the LC-NE system is related to target processing in RSVP, then this should result in a more pronounced AB. The lack of correlation between estradiol levels and the AB moreover suggests that such relationship, if present, might not be linear or that it is modulated by additional hormonal factors. Future research should aim to further explore this idea.

VEP differences between the left and the right hemisphere did not reach significance in the present study. This might be a statistical power issue specific to VEPs, as several ERP effects were replicated numerically and statistically confirmed. That is, T2 items presented in the left visual field were associated with significantly shorter N2pc latencies and larger N2pc and P3 amplitudes as compared to T2 items presented in the right visual field, which matches the findings of Verleger et al. (2011), and which provides further evidence for a LVF advantage for processing rapidly incoming information.

We did not observe a modulation of hemispheric differences in the VEPs by cycle phase. Thus, our data do not provide any evidence in support of the suggestion that estradiol affects the stimulus-specific, bottom-up aspects of lateralization (Hodgetts et al., 2015). Our findings do however indicate that the menstrual cycle can affect the processing of rapid sequences in both hemispheres as reflected in the overall longer P1 latencies during the follicular phase. Latencies of early auditory (Tillman, 2010) and visual potentials (Hausmann et al., 2013) have been reported to vary during the menstrual cycle. There is no clear line in the direction of the results though. For instance, while Hausmann et al. (2013) found that the latency of the right visual N170 to left visual field stimuli was shorter during the luteal phase as compared to the menstrual phase, Tillman (2010) reported that latencies of right hemisphere early auditory ERPs to left ear stimuli were shorter during menses than during follicular phase. The two studies are very different from the present study, but they do show that gonadal steroids can affect stimulus processing at an early stage. The same conclusion can be drawn from the present study for the processing of rapid visual sequences.

Similar to VEPs, hemispheric differences in N2pc or P3 were not affected by menstrual cycle. Thus, our data do also not add supporting evidence to the idea that estradiol primarily modulates the top-down aspects of lateralization (Hjelmervik et al., 2012). Cycle phase did affect the difference between T2 lags though, with a significant difference in T2 evoked P3 latency between lag 2 and lag 7 in the follicular phase only. A P3 peak delay has been previously observed for short as compared to long T1-T2 intervals (Sessa et al., 2007; Vogel and Luck, 2002) and for participants with a pronounced AB as compared to participants

with no AB (Martens et al., 2006). In these studies, it has been suggested that the peak delay reflects a delay in T2 consolidation. Along this line of evidence, our data suggest that target consolidation in rapid serial visual presentation is much less affected by target-to-target interval during the menstrual phase as compared to the follicular phase. It is conceivable that the delay in T2 consolidation for short target-to-target intervals relates to the longer P1 peak latency observed in the follicular phase for distracter evoked VEPs. The finding that the N2pc did not display cycle-related latency effects does not invalidate this possibility as it could be due to the comparatively poor signal-to-noise ratio of the N2pc (Verleger et al., 2011) or that the N2pc only captures aspects of information processing not affected by the menstrual cycle.

As a final remark, whereas 26 women completed the study, only 13 fulfilled all inclusion criteria. We are aware that the rather small final sample size is a limitation of the present study, believe it however to be balanced by the careful control of cycle phase using direct hormone measurements and by the within-participant design.

5. Conclusion

The present study did neither provide evidence for the idea that estradiol reduces in particular the stimulus-driven bottom-up aspect of lateralization and inhibition (Hodgetts et al., 2015) nor for the suggestion that estradiol modulates especially top-down aspects of lateralization (Hjelmervik et al., 2012). The present study showed, however, that early stage stimulus processing in rapid visual sequences is affected by menstrual cycle. It further indicates that the

menstrual cycle affects target consolidation. The cycle-related modulations in behavior and neurophysiology might be due to the interaction of hormonal effects or due to a non-linear effect estradiol exerts on the LC-NE system.

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